[0011] FIG. **5**A and FIG. **5**B depict analysis of a 25 L-scale preparation of an exemplary anti-HER2 biparatopic antibody. FIG. **5**A depicts the SDS-PAGE profile of an exemplary anti-HER2 biparatopic following MabSelect™ and HiTrap™ SP FF purification. FIG. **5**B depicts LCMS analysis of the purified antibody.

[0012] FIG. **6**A-**6**G compare the ability of an exemplary biparatopic anti-HER2 antibodies to bind to HER2+ whole cells displaying different HER2 receptor density compared to control antibodies, as measured by FACS. FIG. **6**A and FIG. **6**E depict binding to SKOV3 cells;

[0013] FIG. **6**B depicts binding to JIMT1 cells; FIG. **6**C and FIG. **6**F depict binding to MCF7 cells; FIG. **6**D depicts binding to MDA-MB-231 cells; and FIG. **6**G depicts binding to WI-38 cells.

[0014] FIGS. **7**A-**7**E depict the ability of exemplary anti-HER2 biparatopic antibodies to inhibit the growth of HER2+ cells. FIG. **7**A and FIG. **7**D show growth inhibition in SKOV3 cells; FIG. **7**B shows growth inhibition in BT-474 cells; FIG. **7**C shows growth inhibition in SKBR3 cells, and FIG. **7**E shows growth inhibition in JIMT-1 cells.

[0015] FIGS. **8**A and **8**B depict the SPR binding data relating to the paratopes of an exemplary anti-HER2 biparatopic antibodies. FIG. **8**A illustrates the K_D values (nM) of a monovalent anti-Her2 antibody (v1040; representing the antigen binding domain on CH-B of exemplary anti-Her2 biparatopic antibody), for binding to immobilized Her2 ECD or dimeric Her2-Fc. FIG. **8**B illustrates the K_D values (nM) of a monovalent anti-Her2 antibody (v4182; representing the antigen binding domain on CH-A of exemplary anti-Her2 biparatopic antibody) for binding to immobilized Her2 ECD or dimeric Her2-Fc.

[0016] FIGS. **9**A and **9**B depict the ability of exemplary anti-HER2 biparatopic antibody to internalize in HER2+ cells. FIG. **9**A depicts internalization in BT-474 cells, while FIG. **9**B depicts internalization in JIMT-1 cells.

[0017] FIGS. **10**A-**10**F depict surface binding and internalization of exemplary anti-HER2 biparatopic antibodies. FIG. **10**A (v5019) depicts the result in BT-474 cells; FIG. **10**B (v5019) and FIG. **10**F (v5019 and v10000) depict the result in JIMT1 cells; FIG. **10**C (v5019) and FIG. **10**E (v5019 and v10000) depict the result in SKOV3 cells, and FIG. **10**D (v5019) depicts the result in MCF7 cells.

[0018] FIGS. **11**A-**11**C depict the ability of an exemplary anti-HER2 biparatopic antibody to mediate ADCC in SKOV3 cells. In FIG. **11**A, the assay was carried out using an effector to target cell ratio of 5:1; in FIG. **11**B, the assay was carried out using an effector to target cell ratio of 3:1; and in FIG. **11**C, the assay was carried out using an effector to target cell ratio of 1:1.

[0019] FIGS. **12**A-**12**C depict the characterization of affinity and binding kinetics of monovalent anti-HER2 (v630 and v4182) and an exemplary biparatopic anti-Her2 antibody (v5019) to recombinant human HER2. FIG. **12**A shows the measurement of ka (1/Ms). FIG. **12**B shows the measurement of kd (1/s). FIG. **12**C shows the measurement of K_D (M).

[0020] FIGS. **13**A-**13**C depict affinity and binding characteristics of an exemplary biparatopic anti-HER2 antibody to recombinant human HER2 over a range of antibody capture levels. FIG. **13**A depicts the measurement of kd (1/s) to HER2 ECD determined over a range of antibody capture levels for exemplary biparatopic anti-Her2 antibody (v5019). FIG. **13**B depicts the measurement of kd (1/s) to HER2 ECD determined over a range of antibody capture levels for monovalent anti-Her2 antibody (v4182). FIG. **13**C depicts the measurement of kd (1/s) to HER2 ECD determined over a range of antibody capture levels for monovalent anti-Her2 antibody (v630).

[0021] FIG. **14** shows a comparison of the mechanism of binding of a monospecific anti-ECD4 HER2 antibody (left), and a Fab-scFv biparatopic anti-ECD2×ECD4 HER2 antibody (right). The monospecific anti-ECD4 HER2 antibody is capable of binding one antibody molecule to two HER2 molecules; whereas the biparatopic anti-ECD2×ECD4 HER2 antibody is capable of binding one antibody to two HER2 molecule, as well as 2 antibodies to one HER2 molecule and combinations therein which results in HER2 receptor cross-linking and lattice formation followed by downstream biological effects such as internalization and/or growth inhibition as indicated by the arrows. IEC represents "immune effector cells." The four extracellular domains of HER2 are numbered as 1, 2, 3, or 4 where 1=ECD1, 2=ECD2, 3=ECD3, and 4=ECD4.

[0022] FIG. **15** depicts the effect of an exemplary anti-HER2 biparatopic antibody on AKT phosphorylation in BT-474 cells.

[0023] FIGS. **16**A-**16**C depict the effect of an exemplary anti-HER2 biparatopic antibody on cardiomyocyte viability. FIG. **16**A depicts the effect of v5019 and the corresponding ADC v6363 on cardiomyocyte viability; FIG. **16**B depicts the effect of v5019, v7091, and v10000 and corresponding ADCs v6363, 7148, 10553 on cardiomyocyte viability, and FIG. **16**C depicts the effect of v5019, v7091, and v10000 and corresponding ADCs v6363, 7148, 10553 on the viability of doxorubicin-pretreated cardiomyocytes.

[0024] FIGS. **17**A-**17**G depict the ability of exemplary anti-HER2 biparatopic antibody drug conjugates to inhibit the growth of HER2+ cells. FIG. **17**A shows the ability of the ADC v6363 to inhibit the growth of JIMT1 cells. FIG. **17**B shows the ability of the ADC v6363 to inhibit the growth of SKOV3 cells. FIG. **17**C shows the ability of the ADC v6363 to inhibit the growth of MCF7 cells. FIG. **17**D shows the ability of the ADC v6363 to inhibit the growth of MDA-MB-231 cells. FIG. **17**E shows the ability of ADCs v6363, v10553, and v1748 to inhibit the growth of SKOV3 cells. FIG. **17**F shows the ability of ADCs v6363, v10553, and v1748 to inhibit the growth of JIMT-1 cells. FIG. **17**G shows the ability of ADCs v6363, v10553, and v1748 to inhibit the growth of NCI-N87 cells.

[0025] FIG. **18**A and FIG. **18**B depict the effect of a biparatopic anti-HER2 antibody in a human ovarian cancer line xenograft model (SKOV3). FIG. **18**A shows the effect of the antibody on mean tumor volume. FIG. **18**B shows the effect of the antibody on percent survival of the animals.

[0026] FIG. **19**A and FIG. **19**B depict the effect of a biparatopic anti-HER2 antibody drug conjugate (ADC) in a human ovarian cancer line xenograft model (SKOV3). FIG. **19**A shows the effect of the antibody on mean tumor volume. FIG. **19**B shows the effect of the antibody on percent survival of the animals.

[0027] FIG. **20** depicts the effect of a biparatopic anti-HER2 antibody drug conjugate (ADC) on mean tumour volume in a human breast primary cell xenograft model (HBCx-13b).